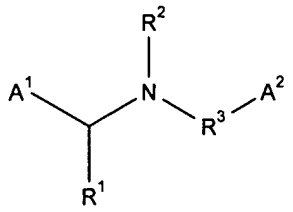
REMARKS/ARGUMENT

Claims 1 through 9, 11, and 13 through 22 are pending in the application. Claims 10, 12, and 18 are canceled, claims 1, 11, 15 through 17, and 19 are amended, and new claims 21 and 22 are added. Entry of these amendments is respectfully requested as it is believed they put the application in condition for allowance or in better condition for appeal.

1. Rejection under 35 U.S.C. § 103(a)

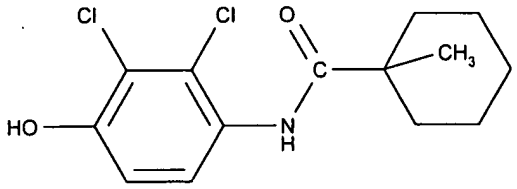
Claims 1 through 20 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Moloney et al. (WO 99/42447) in view of Brandes et al. (U.S. Patent No. 5,532,262).

Moloney et al. disclose compounds of formula (I)



and salts thereof as phytopathogenic fungicides wherein A^1 is substituted 2-pyridyl; A^2 is optionally substituted phenyl; R^3 is -(C=O)-, $-SO_2-$ or -(C=S)-; R^1 is hydrogen, optionally substituted alkyl or acyl; and R^2 is hydrogen or optionally substituted alkyl are useful phytopathogenic fungicides.

Brandes et al. merely disclose that a compound of the formula:



which is nothing at all like the pyridylethylbenzamide derivatives employed in the practice of the present invention, can be combined with known fungicidal active compounds, such as carbendazim and/or diethofencarb and/or iprodione and/or benomyl, among others.

It is understood to be the Examiner's position that Compound (I) is a known fungicide and carbendazim is a known fungicide (as are diethofencarb, iprodione, thiophanate, thiophanate-methyl, and benomyl) and, thus, it would be obvious to use them in combination.

The Applicants acknowledge that compounds of the 2-pyridylethylbenzamide type, which are employed in the compositions of the present invention, have fungicidal action and are disclosed and claimed in co-pending U.S. Patent Application Serial No. 10/524,345, filed February 11, 2005, (U.S. Pub. No. 2005/0234110) and also acknowledge that carbendazim is a known fungicide, too. However, it is the Applicants' position that they have discovered a combination that clearly exhibits synergism and is neither disclosed nor suggested by the cited art. They have demonstrated this synergism for this combination in Example 1, using means for determining synergism that is accepted in the art, i.e., the Colby formula, which was published in the journal 15 WEEDS 20-22 (1967). The Examiner's attention is directed to U.S. Patent No. 6,753,339 in which the Colby method of determining synergism was also employed to the

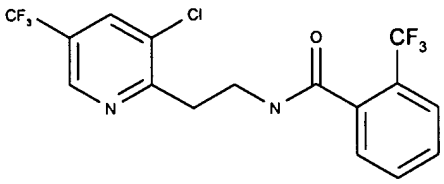
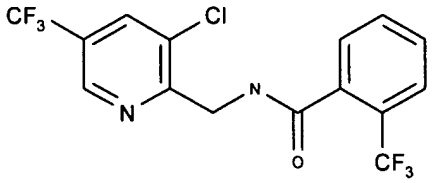
satisfaction of the Patent Office. Based on the teachings of the two cited references, skilled artisans might have expected fungicidal activity for mixtures of a 2-pyridyl*methyl*benzamide, e.g., 2,6-dichloro-N-{[3-chloro-5- (trifluoromethyl)-2- pyridinyl] *methyl*} benzamide, and carbendazim, but they would not have expected any synergy when associating these compounds and, in particular, would not have expected the synergy between the 2-pyridyl*ethyl*benzamides, e.g., N-{2-[3-chloro-5-(trifluoromethyl)-2-pyridinyl]*ethyl*}-2-trifluoromethylbenzamide, and the carbendazim evidenced by the example of the present application. Unexpected results have been shown for the claimed combination, and it logically follows that the combination cannot be obvious.

Additionally, in the prosecution of co-pending U.S. Patent Application Serial No. 10/524,345, referred to above, the Examiner stated:

> The difference between the prior art [i.e., Moloney et al.] compound and the instantly claimed compound is the alkylene group between the pyridyl group and the benzamide moiety. In the instant compound, alkylene group is ethylene. In the prior art compound, alkylene group is a methylene group. The prior art compound and the instant compound are homologues of each other. Homologues are compounds that differ by a methylene linkage. Here, the Moloney compounds are also fungicides as are the instant compounds. See line 4 of page 2.
>
> It would have been obvious to one of ordinary skill in the art to synthesize homologues of this class of compounds and compositions. Accordingly, the compounds are deemed unpatentable therefrom in the absence of a showing of unexpected results for the claimed compounds over those of the generic prior art compounds.

The Applicants in that case submitted in response the following experimental data to show unexpected results that demonstrate the benefits in terms of fungicidal activity of an

ethylene group linking the pyridyl and benzamide moiety with each other, rather than a *methylene* group:

Compound		*Botrytis cinerea*	*Alternaria brassicae*
According to the invention		Good to very good activity (80-100%) at 330 ppm	Good to very good activity (80-100%) at 330 ppm
Compound 1 of U.S. 6,503,933 (Moloney et al.)		No activity at 330 ppm	No activity at 330 ppm

The Applicants in that case argued that this finding would have been surprising to persons of ordinary skill in the art and would not have been rendered obvious by Moloney et al., and submitted a Declaration Under Rule 132 in support of the data.

Thus, in the present application, the Applicants have discovered a novel and unobvious combination of fungicides that exhibits a synergistic effect that allows a reduction of the chemical substances spread into the environment and a reduction of the cost of the fungal treatment. The combination of the present invention enables a reduction in the doses of chemical products spread in the environment in order to control fungal attacks of crops, in particular by reducing the doses of the products for application, and increases the number of antifungal

products available to farmers for them to find among them the fungicidal agent best suited to their particular use. These advantages are neither taught nor disclosed by the cited art.

The Examiner has stated on page 6 of the current Office Action:

> The present claims are drawn to a combination of formula (I) and a compound capable of inhibiting mitosis and cell division. The specification only provides enablement for the combination of N-{243-chloro-5-(trifluoromethyl)-2-pyridinyllethy1}-2 trifiuoromethylbenzamide and carbendazim in a ratio of 1:1. However, the results appear to show an additive effect. For example, where the dosage is 125 +125 of compound 1:Carbendazim, 63 +16=79, which is an expected result of adding the efficacy values.

It is respectfully submitted the Examiner has made two errors in this paragraph.

First, if the Examiner is taking the position that the currently claimed invention is unpatentable for lack of enablement, the proper grounds for rejection are 35 U.S.C. § 112, paragraph 1, not 35 U.S.C. § 103. Further, it is submitted that, at the very least, current claims 19 and 21 are reflections of Example 1 of the application and are undeniably enabled thereby.

Second, with regard to the results shown in Example 1 appearing to show only an additive effect, it is believed the Examiner has made a mathematical error. As noted in the specification of the current application, the expected percentage of inhibition is defined in the Colby method for determining synergism as E=x+y - [(x*y)/100]. In the portion of Example 1 referred to by the Examiner, x=63 and y=16. Thus, E=63+16 - [(63*16)/100], or 79 - 10.08, or, rounding off, 69. However, for the combination of the present invention, the efficacy was found to be 79, showing a synergism (Colby) of +10, as shown in Example 1.

Accordingly, it is requested that the rejection of claims 1 through 20 under 35 U.S.C. § 103(a) as being unpatentable over Moloney et al. in view of Brandes et al. be withdrawn.

2. Supplement to the Applicants' Previous Response

In the course of prosecuting an application (U.S. Patent Application No. 10/588,532, filed October 12, 2006) similar to the current application, it has been necessary to reconsider the teaching of Cooke et al., U.S. Patent No. 6, 821, 992, which was cited by the Examiner in the current application in an Office Action dated February 27, 2008.

In the March 16, 2009, response to the Office Action of December 17, 2008, it was stated:

> Claims 1-15 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Cooke et al. in view of Brandes et al. (U.S. Patent No. 5,532,262), and Hammond et al. (Exploring the mechanisms of action of FB642 at the cellular level, 2001).
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> Cooke et al. disclose compounds of general formula I,
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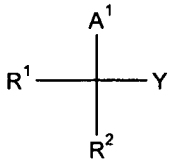
> 
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>
> where A^1, R^1, R^2 and Y are as defined in the description; and to their use as phytopathogenic fungicides.
>
> It has been pointed out in the second paragraph of the present specification that international patent application WO 01/11965 (an equivalent of U.S. Patent No. 6,821,992) generically discloses numerous pyridylethylbenzamide derivatives and that the possibility of combining one or more of these numerous pyridylethylbenzamide derivatives with known fungicidal products to develop a

fungicidal activity is disclosed in general terms, without any specific example or biological data.

It is submitted, however, that a pyridylethylbenzamide derivative having the general formula (I) of the present application is neither disclosed not suggested by Cooke et al.

The structure of general formula (I) of the present invention includes a four atom linking group (to use the terminology of Cooke et al.) between the pyridine ring and the phenyl ring, with the pyridine ring being directly attached to a carbon atom, i.e. a CH_2 group.

Cooke et al. teach that Y is either an -L-A^2- moiety or an -L^1-A^3- moiety, where L is a three atom linker and L^1 is a four atom linker. Thus, since the compound employed in the practice of the present invention comprises a four atom linker, only the -L^1-A^3- moiety of Cooke et al. needs to be considered. An examination of the definition of L^1 in column 1 of Cooke et al. beginning at line 45, however, reveals that in all cases, the atom directly attached to the pyridine group is nitrogen, not carbon, i.e., -N(R^9)C(=X)-X^1-CH(R^7)-, -N(R^9)C(=X)CH(R^7)CH(R^8)-, -N(R^9)C(=X)C(R^7)=C(R^8)-, -N(R^9)C(R^7)=C(R^8)-C(=X)-, -N(R^9)C(R^7)=C(R^8)-SO_2-, -N(R^9)C(=X)C(R^7)(R^8)-SO_2- and -N(R^9)C(=X)C(R^7)(R^8)-X^1-; wherein A^1, the pyridine ring, is *attached to the left hand side of linker L*^{1}. Thus, it is clear that the compounds disclosed by Cooke et al. do not read on the pyridylethylbenzamide derivatives employed in the practice of the present invention.

Upon further consideration, it appears that, although unclear, the Patentees may not have intended that A^1 was directly attached to the left hand side of linker L^1, but, rather, were saying that A^1 was to the left of L^1 with a group C(R^1)(R^2), which could, *inter alia*, be -CH_2-, intervening. If that was the intended teaching, then in the current application, the "linker" would be one having three atoms in Cooke et al.'s terminology, i.e., -CH_2-NH-C(=O)-, and would be read on by the group -CH(R^3)N(R^5)C(=X)- in column 1 of Cooke et al. at line 42. This would be

in accordance with the present Applicants' teaching referred to in the above quotation that U.S. Patent No. 6,821,992 generically discloses numerous pyridyl*ethyl*benzamide derivatives.

The fact remains, however, that there is no teaching or suggestion in Cooke et al. of the synergistic effect obtained when these pyridylethylbenzamide derivatives are combined with compounds capable of inhibiting mitosis and cell division, such as carbendazim.

It was further pointed out in the response to the Office Action dated February 27, 2008, that the secondary references, Brandes et al. and Hammond et al., failed to supplement the deficiencies, as a reference, of Cooke et al. It was stated:

> Brandes et al. merely disclose that a compound of the formula:
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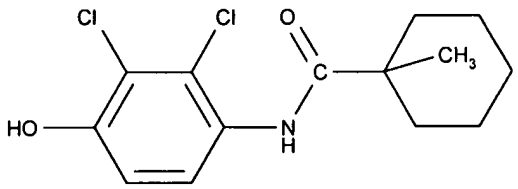
> 
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>
> which is nothing at all like the pyridylethylbenzamide derivatives employed in the practice of the present invention, can be combined with known fungicidal active compounds, such as carbendazim and/or diethofencarb and/or iprodione and/or benomyl, among others.
>
> Hammond et al. do nothing more than teach that carbendazim is a known fungicide. There is no mention of its use in combination with anything resembling the pyridylethylbenzamide derivatives employed in the practice of the present invention.

These arguments are hereby reiterated.

3. Conclusion

In view of the foregoing, it is submitted that this application is in condition for allowance, and an early Office Action to that end is earnestly requested.

Respectfully submitted,

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